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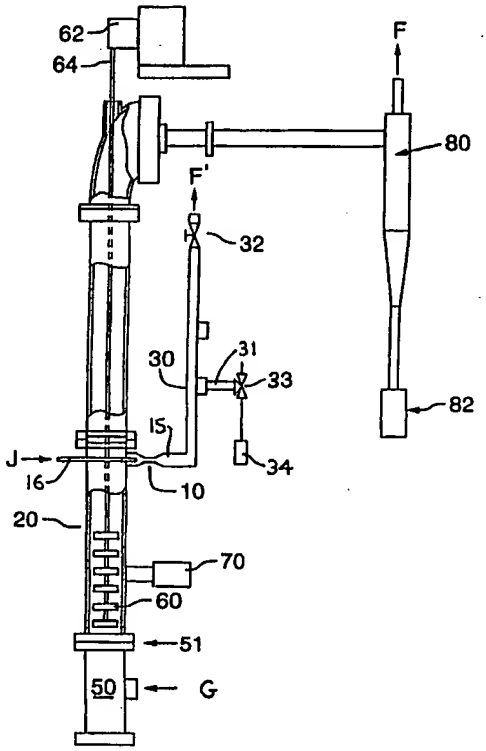
(54) Title: APPARATUS FOR PRECISELY DISPENSING SMALL AMOUNTS OF ULTRA–FINE PARTICLES

(57) Abstract

A dispensing apparatus is provided for the dispensing of fine particles on a dry basis in a reproducible manner, using two–stage fluidization of particles. The first stage (20) is preferably a fluidized bed with a freeboard on the top, but possibly a dilute–phase fluidized bed with a dilute gas–solids suspension filling the whole chamber, and the second stage (30) is a dilute gas–solid suspension fluidized bed. The second stage receives particles drawn from suspended particles in the first stage (20), and produces a very uniform dilute suspension of those particles, from which very accurate quantities can then be drawn via withdrawal ports (31), into a collection area (34) for dispensing therefrom. Optionally, multiple second–stage chambers can be provided, each drawing suspended particles via a separate conduit (15) from the first–stage chamber (20), which is potentially much larger. Similarly, there could be multiple withdrawal ports (31) from each second–stage chamber, to increase the total number of dispensing points (34). Withdrawal is preferably by time–controlled opening of the withdrawal port or ports, resulting in accurate dispensing proportional to the length of time.



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APPARATUS FOR PRECISELY DISPENSING SMALL AMOUNTS OF ULTRA-FINE PARTICULES

TECHNICAL FIELD

This invention relates to the accurate dispensing of very small quantities of ultra-fine particles in a reproducible manner.

In the pharmaceutical industries (and also other industries), it is often necessary to accurately dispense very small quantities (in the order of 1 mg or less) of ultra-fine (< 10 μm) pharmaceutical (or other) particles on a dry basis in a reproducible manner. For example, very fine particles are administered to patients by means of inhalation. Higher potency of these new drug compounds requires much smaller doses than in previous dispensing applications. The existing equipment available commercially typically can only dispense an amount in the order of 5 ± 0.5 mg. It would be desirable to be able to dispense quantities of 1 mg or less with a spread of ±0.1 mg or less.

BACKGROUND ART

The inventors are not aware of any available technology to dispense such small quantities of ultra-fine particles on a dry basis. For quantities larger than 5 mg, several types of solids feeding systems have been developed over the years. Among them are feeders designed to deliver particles at flowrates of the order of 1 kg/h for laboratory and pilot scale gas-solid reactions (e.g. combustion, gasification, catalytic reactions and metallurgical processes). The most common kind of solids feeder is a mechanical feeder such as a belt or screw conveyor. However, mechanical feeders are generally inefficient and unreliable in feeding very fine particles in particular, due to the cohesive properties of the powder which prevent free motion of solids and lead to difficulty in transporting the powder.

A fluidized bed feeder as a non-mechanical solids feeder would have the potential to dispense smaller quantities with suitable reproducibility. While there are several types

of conventional fluidized bed feeders developed, none of them is suitable for the required small quantities and ultra-fine particles. None of the prior art feeders known to the inventors can dispense the very small quantity of fine particles of interest here.

Processing of fine particles (including nanometer particles) has been identified by governments and industries as one of the key development areas for the 21st century.

To accurately dispense ultra-fine particles, all mechanical methods are expected to fail due to the cohesive nature of the ultra-fine particles. Existing conventional solids feeders cannot handle the small quantities of particles for drug doses of the order of 1 mg or less.

DISCLOSURE OF INVENTION

It is an object of the invention to accurately dispense very small quantities of ultra-fine particles, such as pharmaceuticals for example, on a dry basis in a reproducible manner.

In the invention, there is two-stage fluidization of particles. The first stage is preferably a fluidized bed with a freeboard on the top, but possibly a dilute-phase fluidized bed with a dilute gas-solids suspension filling the whole chamber, and the second stage is a dilute gas-solid suspension fluidized bed. The second stage receives particles drawn from suspended particles in the first stage, and produces a very uniform dilute suspension of those particles, from which very accurate quantities can then be drawn. Thus the invention has first-stage and second-stage gas-solids suspension or fluidization chambers, each having particle fluidization means, and a conduit connecting the first-stage and second-stage chambers, for flow of suspended particles from the first-stage chamber to the second-stage chamber. A pressure differential is created between the first-stage and second-stage chambers, by means such as a Venturi for example, to transfer suspended particles from the first-stage chamber into the second-stage chamber via the conduit. For accurate dispensing purposes, suspended particles

are drawn from the second-stage chamber via withdrawal ports, into a collection area for dispensing therefrom.

If desired, multiple second-stage chambers can be provided, each drawing suspended particles via a separate conduit from the first-stage chamber, which is potentially much larger. Thus in an industrial setting, there could be a quite large first-stage chamber, with conduits extending to many second-stage chambers at remote locations.

Similarly, there could be multiple withdrawal ports from each second-stage chamber, to increase the total number of dispensing points.

One application of this new fluidized dispensing system is in the pharmaceutical industry to dispense very small doses for drug administration. This technology can also find applications in many other industries when the metering of small quantities of particles is required.

One advantage of this invention is that accurate dispensing of small quantities of fine particles is achieved using cost-effective pneumatic rather than mechanical means.

Although the invention is well-suited for ultra-fine particles and for small quantities, the invention can also handle larger particles and quantities of larger than 1 mg, up to the point where other more conventional methods begin to work more effectively, for example in the 100-200 mg range. However, the smaller the particles the more difficult it is to dispense them using conventional methods. The application of the invention is, therefore, not to be construed as one that is strictly limited to dispensing only very small quantities of the order of 1 mg or less, and ultra-fine particles, although that is where the invention is potentially most useful.

Although the first-stage chamber stage in the preferred embodiment of the invention is a dense-phase fluidized bed with a freeboard on the top, it should be appreciated that the first stage could instead also be a dilute-phase fluidized bed with a dilute gas-solids suspension filling the whole chamber.

Further features of the invention will be described or will become apparent in the course of the following detailed description.

BRIEF DESCRIPTION OF DRAWINGS

In order that the invention may be more clearly understood, preferred embodiments thereof will now be described in detail by way of example, with reference to the accompanying drawings, in which:

Fig. 1 is a schematic overview of the dispensing system;

Fig. 2 is a close-up view of the first embodiment of the Venturi area of the dispensing system, shown in section;

Figs. 3-9 are various views illustrating alternative Venturi arrangements; and

Fig. 10 is a schematic close-up view of the dilute particle withdrawal configuration.

BEST MODE FOR CARRYING OUT THE INVENTION

Fig. 1 illustrates the preferred embodiment of the system. There is a first-stage gas-solids fluidization chamber **20** in which loaded particles are fluidized by any suitable conventional means to form a suspension of particles, for example via a fluidizing gas **G** introduced through a windbox **50** and a perforated-plate air distributor **51** clamped between two flanges. Preferably but not necessarily in every case, fluidization aids may be used, such as six impellers **60** positioned within the fluidization bed to stir the dense phase in order to improve the fluidization quality of the very fine particles, the impellers being mounted onto a shaft **64** driven by a mechanical stirrer **62**. A vibrator **70** of variable frequency, such as a pneumatic turbine, may also be mounted on the outer

wall of the main column to aid in fluidizing the fine cohesive particles. Other fluidization aids could also be employed as required or desired, including the "Gaseous Fluidization Aids" described in co-pending international patent application no. PCT/CA99/_____ of that title, filed August 13, 1999, claiming priority from U.S. patent application ser. no. 09/133,215, these applications being hereby incorporated by reference.

A conduit **15** connects a freeboard area **41** (i.e. the area above the bed of powders **40** where there is a suspension of particles - see Fig. 2) of the first-stage chamber **20** to a second-stage gas-solids fluidization chamber **30** for flow of suspended particles from the first-stage to the second-stage chamber. A pressure differential is created between the first-stage and second-stage chambers, by means such as a Venturi **10** in the conduit **15** for example, fed by a high speed gas stream **J** (having a velocity in the order of 10 - 50 m/s, for example) introduced via a gas feed tube **16** to produce the desired Venturi effect and thus the desired flow of suspended particles from the first-stage chamber into the second-stage chamber. From the second-stage chamber **30**, where there is a much more uniform and dilute suspension of the particles than in the first-stage chamber, by virtue of a steady dilute flow of particles being maintained, suspended particles are withdrawn via a withdrawal tube **31** into a collection cell **34**, as will be described in greater detail below.

This two-stage fluidization results in extremely accurate dispensing, since a dilute, very stable and very uniform suspension is achieved in the second-stage chamber. Accurate, reliable and reproducible quantities are obtained, such that in production, once operating conditions are set and calibrated, only periodic checking of collected amounts for purposes of quality control monitoring should be required.

As mentioned above, multiple "second" chambers **30** can be provided, each drawing suspended particles via a separate conduit **15** from the first-stage chamber, which is potentially much larger. For clarity of illustration and explanation, this description focuses on the situation where there is only a single second-stage chamber, but it should be clearly understood that multiple second-stage chambers are also contemplated. The separate conduits **15** would draw from different points around the

circumference of the first-stage chamber, at the same height or at different heights as desired.

As also mentioned above, it should be equally clear that the second-stage chamber **30**, or each second-stage chamber **30** if more than one, could have multiple withdrawal tubes **31**. Again for clarity of illustration and explanation, this description focuses on the situation where there is only a single withdrawal tube.

Although this description is specifically with respect to a Venturi and a high velocity gas stream therein to create the desired Venturi effect, it should also be understood that any form of conduit in which a pressure difference between the first-stage fluidization chamber and the second-stage fluidization chamber is provided, so as to result in lower pressure in the second-stage chamber and hence flow from the first-stage chamber to the second-stage chamber, would be suitable in this invention. For example, a vacuum (not shown) could be disposed in the general area at the upper end of the second-stage fluidization chamber **30**, to provide a lower pressure in the conduit. Alternatively, the first-stage fluidization chamber may be pressurized to a pressure greater than the second-stage fluidization chamber or chambers.

Figs. 3-9 show examples of alternative configurations which can be used with a Venturi to draw suspended particles from the first-stage chamber **20**. Figs. 3 and 4, for example, show the conduit **15** having an end plate **14** which has several orifices **12** therethrough to draw particles from the first-stage chamber. The plate acts to control the mass flow rate of particles diverted to the second-stage chamber. A central opening **13** is also provided, to accommodate the high speed gas feed tube **16**. This is essentially the configuration also shown in Figs. 1 and 2 in less detail.

In the alternative Venturi arrangement shown in Figs. 5-6, the orifices **12** are drilled into the wall of the conduit **15** where it extends slightly into the first-stage chamber **20**. The first embodiment is advantageous in that a variety of orifice numbers and sizes may be used without changing the Venturi apparatus.

Fig. 7 illustrates a setup in which Venturi **10** neck is positioned within the first-stage chamber **20**, with the orifices **12** being at the neck.

Fig. 8 shows tubes **11** intersecting the conduit **15** in the first-stage chamber **20**, the resulting reduced cross-sectional area thus creating a Venturi effect. The tubes **11** draw the suspended particles into the conduit, the outer ends of the tubes acting as the orifices **12**.

Fig. 9 shows a similar arrangement to that of Fig. 8.

Preferably in each case, depending on the application, the orifices **12** are about 1-5 mm in diameter.

Preferably, the Venturi is positioned at a high location in the freeboard. It should be understood that a variety of positions may be suitable for the Venturi, as long as the conduit will draw diluted particles from the freeboard of the dense particle bed in the first-stage chamber. However, in some cases when larger quantities are being metered, it may be necessary to have the conduit draw from or close to the dense bed to increase the flow rate.

A high efficiency cyclone **80** is preferably installed at the exit of the first-stage chamber **20**, to capture particles carried out by the fluidizing gas stream **F** (i.e. from **G**), so that they are not lost. The captured particles are collected in a container **82**, and if desired, may be reintroduced to the bottom of the particle bed in the bottom of the first-stage chamber. If preferred, the cyclone or any suitable form of particle filtering system instead could be placed within the freeboard.

The dilute gas-particle fluidization flow from the second-stage chamber **30** is not returned to the main fluidization column, i.e. the first-stage chamber **20**, to ensure that there is enough pressure drop between the inside of the Venturi and the freeboard of the dense fluidized bed and to thereby to provide smooth flow of particles from the main fluidized bed column into the Venturi. Instead, the gas-particle suspension preferably

is passed through a filter (not shown) to catch the fine powder while the air is released to the atmosphere. This flow of the gas-particle suspension is illustrated by the arrow marked **F'**. In a commercial setup, the separated particles would likely be returned to the first-stage chamber. Preferably, a butterfly valve **32** is installed at the exit of the second-stage chamber. This valve is normally open during the operation of the system, but could be closed periodically and a source of air could be introduced into the column to force the air to flow back into the dense bed periodically so as to purge the Venturi, to prevent the orifices **12** from becoming blocked by the fine particles.

To control the moisture level of the air, the two gas streams (**G** and **J**) may be, preferably, first passed through two separate packed bed adsorption tubes containing a desiccant such as silica gel.

The manner in which the suspended particles are withdrawn via the withdrawal tube **31** into a collection cell **34** will now be described in greater detail. When the withdrawal tube **31** is open, a small quantity of powder suspension will flow out of the second-stage chamber given the positive pressure inside the second-stage chamber. By adjusting the opening period of the withdrawal tube, the amount of powder withdrawn can be accurately controlled. When multiple withdrawal tubes are provided, the productivity can be increased significantly.

A schematic of the preferred particle withdrawal system is shown in Fig. 10. The withdrawal of particles is controlled by a three-way solenoid valve **33** and a timer (not shown). Line **A** and the withdrawal tube **31** are initially open while line **C** is closed by the solenoid valve, so that back-purging gas from line **A** flows into the dilute fluidization column, preventing the particles from entering the withdrawal tube **31**. At the start of the withdrawing sequence, line **C** is opened and line **A** is closed by the three-way solenoid valve **33**. As soon as the flow of purging gas is stopped, the gas-solids suspension begins to flow out of the dilute bed **30** into the withdrawal tube **31** and thence into the collection cell **34**. This flow is caused by the small pressure difference between the dilute fluidization column and the outside, and can be enhanced by applying a suction pressure (vacuum) at the end of the withdrawal train. A predetermined amount of

particles is dispensed simply by controlling the amount of time the solenoid is open. As mentioned above, this can be readily controlled and calibrated to produce a highly accurate, reliable and reproducible quantity.

An alternative withdrawal apparatus (not shown) would be a two-way solenoid valve installed in a single-tube line connecting the dilute phase column and the collection cell. The solenoid valve would be closed when there is no withdrawal and open during the withdrawal process. Purging would become unnecessary when the withdrawal frequency is very high.

Experimental results using lactose powder, for example, show that with appropriate operating conditions it is possible to achieve good quality fluidization for the lactose powder with the aid of internal stirring and/or external vibration and/or other fluidization aids and to achieve good reproducibility of the lactose withdrawal quantities from the dilute fluidization column connected to the main fluidized bed through the Venturi off-take.

It will be appreciated that the above description relates to the preferred embodiment by way of example only. Many variations on the invention will be obvious to those knowledgeable in the field, and such obvious variations are within the scope of the invention as described and claimed, whether or not expressly described.

INDUSTRIAL APPLICABILITY

The invention provides improved dispensing of powders.

CLAIMS:

1. Apparatus for dispensing dry particles, comprising:

a first-stage gas-solids fluidization chamber and at least one second-stage gas-solids fluidization chamber, each first-stage and second-stage chamber having particle fluidization means for creating a suspension of said particles within said chambers;

for each said second-stage chamber, a conduit connected for particles to flow from said first-stage chamber to said second-stage chamber for suspension in said second-stage chamber;

means for providing a pressure drop from said first-stage chamber to each said second-stage chamber, to produce said flow of particles from said first-stage chamber to said second-stage chamber; and,

for each said second-stage chamber, means for withdrawing suspended particles from said second-stage chamber into at least one collection area.

2. Apparatus as recited in claim 1, wherein said conduit is connected for said particles flowing from said first-stage chamber to said second-stage chamber to be particles suspended in said first-stage chamber.

3. Apparatus as recited in claim 1, wherein there are more than one second-stage chambers.

4. Apparatus as recited in claim 1, wherein there are multiple said means for withdrawing suspended particles from each said second-stage chamber, into corresponding multiple collection areas.

5. Apparatus as recited in claim 1, wherein said means for withdrawing suspended particles from said second-stage chamber into a collection area comprises ...

6. Apparatus as recited in claim 1, wherein said second-stage chamber has a dilute-phase fluidized bed with a dilute gas-solids suspension filling the whole chamber.

7. Apparatus as recited in claim 6, wherein said first-stage chamber has a dense-phase fluidized bed with a freeboard above said bed.

8. Apparatus as recited in claim 6, wherein said first-stage chamber has a dilute-phase fluidized bed with a dilute gas-solids suspension filling the whole chamber.

9. Apparatus as recited in claim 1, wherein said means for providing a pressure drop from said first-stage chamber to each said second-stage chamber is a Venturi in each said conduit, supplied with a high velocity gas to create a Venturi effect.

10. Apparatus as recited in claim 1, wherein said means for providing a pressure drop from said first-stage chamber to each said second-stage chamber is by pressurizing said first-stage chamber above a pressure level of each said second-stage chamber.

11. Apparatus as recited in claim 1, wherein said means for withdrawing suspended particles from said second-stage chamber into at least one collection area comprises, for each said collection area, a withdrawal conduit connected between said second-stage chamber and said collection area, with a pressure drop from said second-stage chamber to said collection area, and with a valve between each said withdrawal conduit and collection area, such that flow of particles from said second-stage chamber to said collection area is controlled by said valve.

12. Apparatus as recited in claim 11, wherein said valve is a time-controlled solenoid valve.

13. Apparatus as recited in claim 12, wherein said solenoid valve is a three-way valve with its three ports connected respectively to said withdrawal conduit, said collection area and a higher-pressure purging gas supply, such that purging gas may back-flow in said withdrawal conduit towards said second-stage chamber, thereby preventing suspended particles from entering the withdrawal tube until said three-way valve is operated to connect said withdrawal tube to said collection area instead of to said purging gas supply.

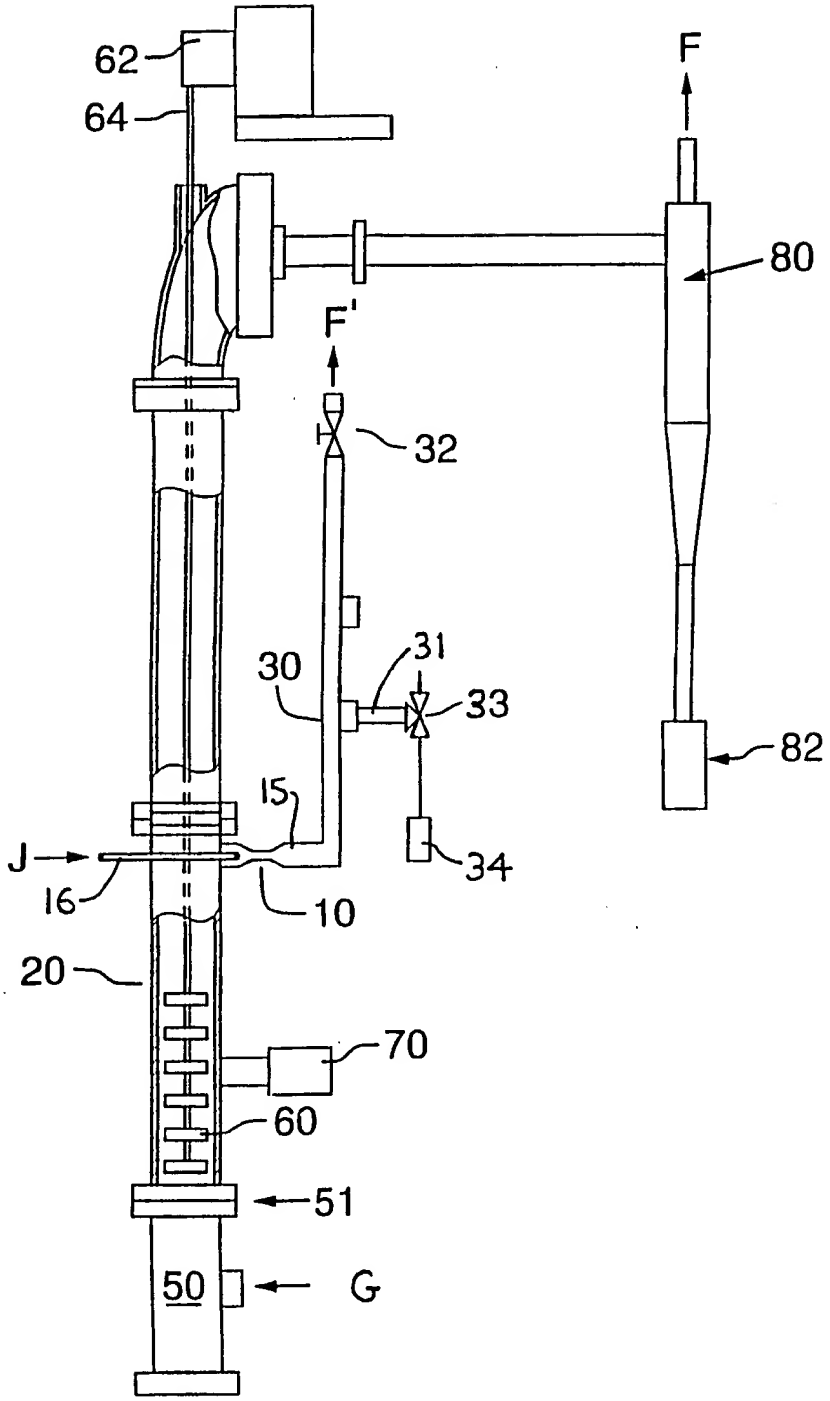

FIG.1

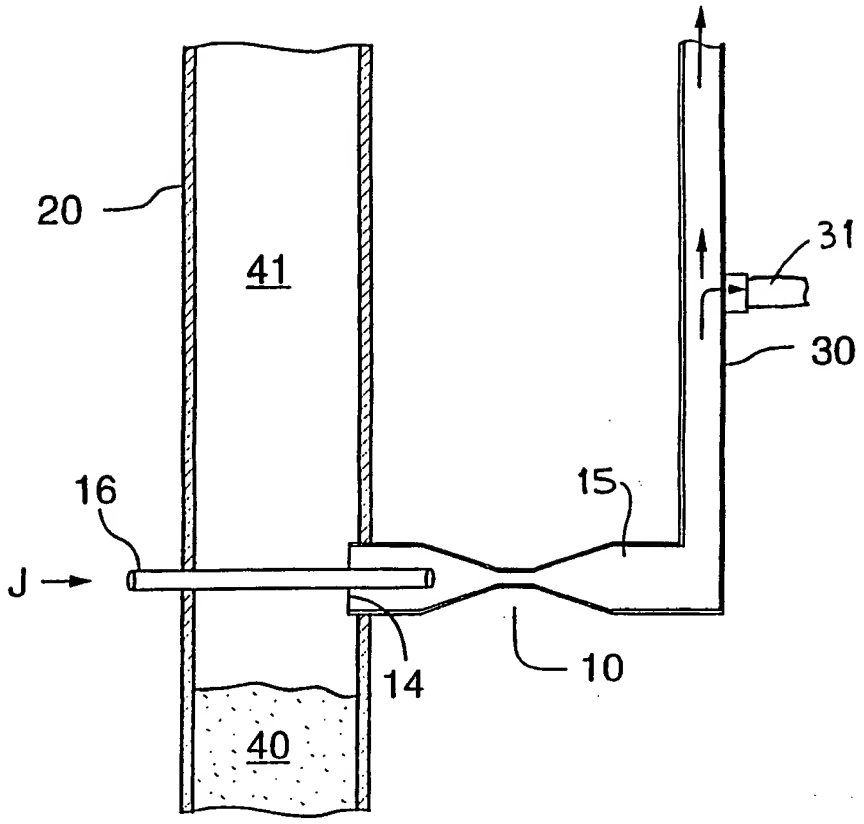

FIG.2

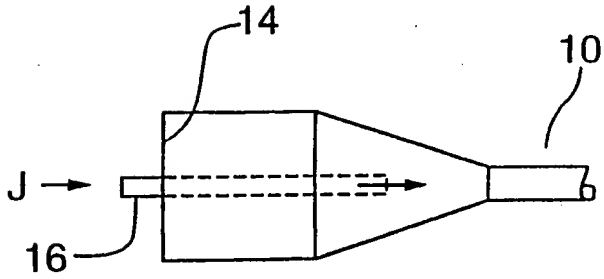

FIG.3

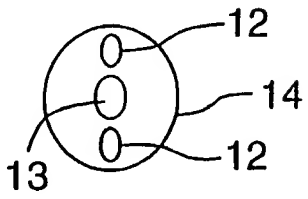

FIG.4

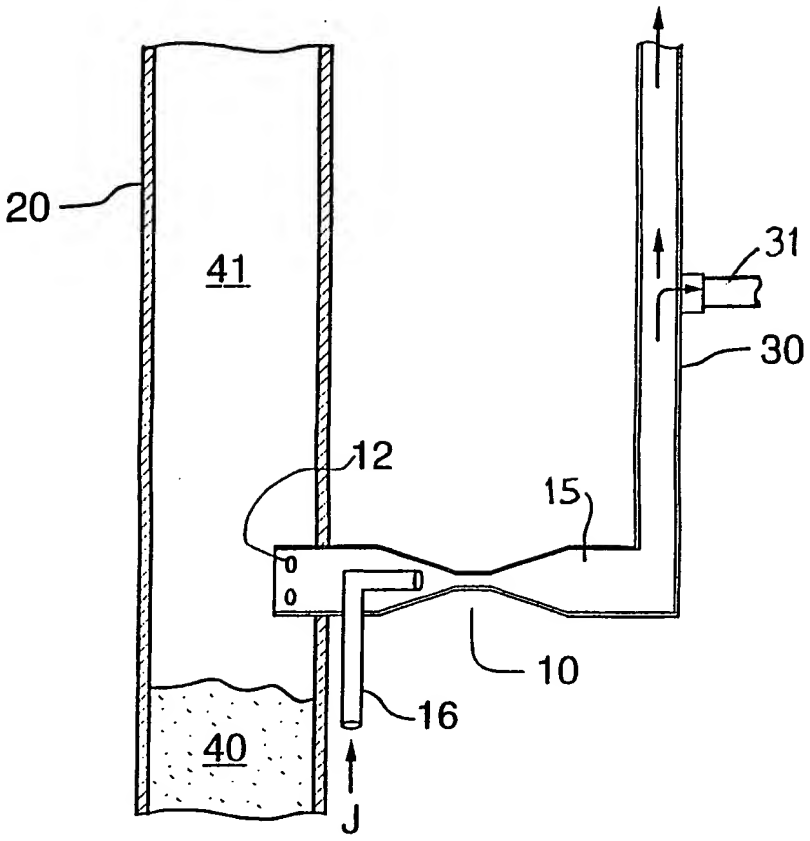

FIG. 5

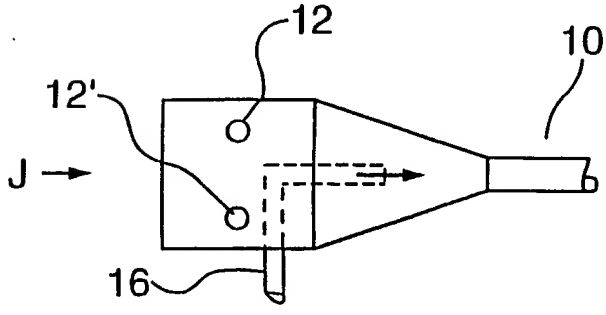

FIG. 6

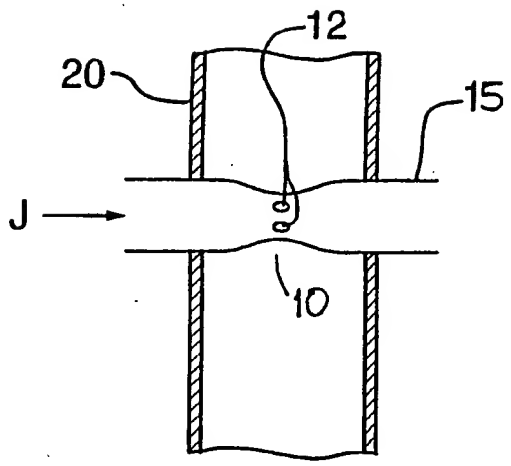

FIG. 7

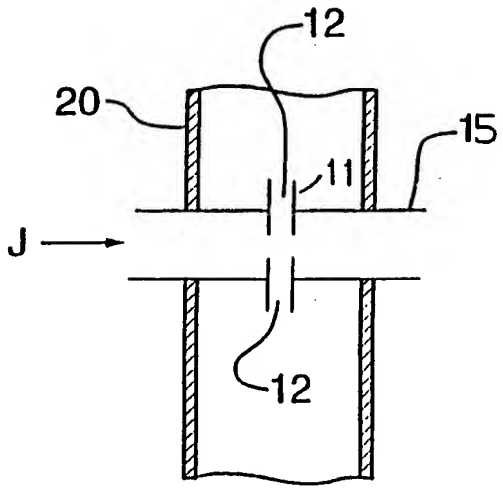

FIG. 8

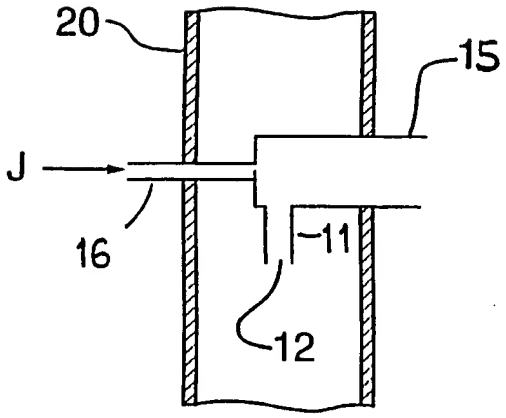

FIG. 9

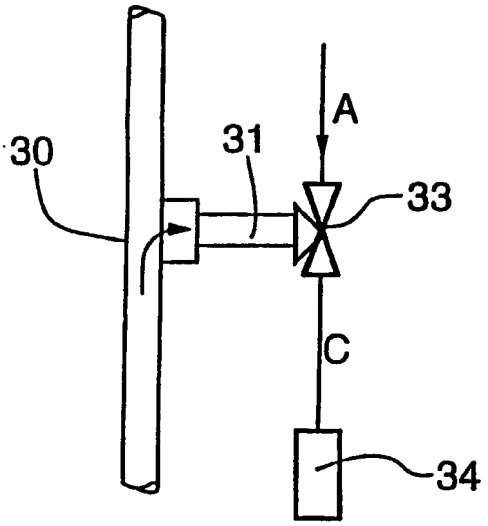

FIG. 10

INTERNATIONAL SEARCH REPORT

Int ional Application No
PCT/CA 99/00743

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 B01F3/06 A61M13/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 B01F A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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A	PATENT ABSTRACTS OF JAPAN vol. 013, no. 107 (C-576), 14 March 1989 (1989-03-14) & JP 63 283728 A (CHUO KAKOKI KK), 21 November 1988 (1988-11-21) abstract ---	1
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[X] Further documents are listed in the continuation of box C.

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Date of the actual completion of the international search	Date of mailing of the international search report
25 November 1999	13/12/1999

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